DRUG ADULTERATION

IN PREHOSPITAL EMERGENCY MEDICAL SERVICES

A Report of Findings in Science, Law and Government

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PREFACE

In the nearly 30-year history of modern emergency medical services (EMS), and estimated 20 million Americans have been administered pharmaceuticals in the prehospital setting. Despite the existence of laws, regulations, scientific evidence, industry standards and industry practice concerning drug adulteration and the requirements for the safe and legal storage of pharmaceuticals, the EMS industry has been unable to establish, control, monitor and guarantee the stability and efficacy of the drugs administered to the American public.

EMS regulatory agencies, physicians, provider organizations and prehospital medical personnel either have been unaware of or have failed to enforce or comply with these laws, regulations and standards. Most importantly, the American public, who expects EMS providers to administer safe and effective pharmaceuticals, is unaware of the problems associated with the administration of adulterated drugs.

This report demonstrates the complex and multi-disciplinary nature of this public health problem. Findings derived from science, practice, law and government drive our recommended comprehensive reform. In 1995, some 800,000 more Americans will receive some form of prehospital drug – the identity, strength, purity and efficacy of which cannot be established, maintained or assured. The EMS community must take immediate steps to eliminate this unacceptable public health problem.

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I. MAGNITUDE AND CHARACTERISTICS OF THE PROBLEM

The emergency medical services industry in the United States was first recognized as an underdeveloped component of the American health care system in 1966, with the issuance of a white paper entitled “Accidental Death and Disability: The Neglected Disease of Modern Society.”[1] The document focused public attention on the need to improve the quality of prehospital and inhospital emergency medical care as a means to reduce morbidity and mortality associated with accidents and serious illness.

Congress passed the Emergency Medical Services Act of 1973, which led to the identification of over 300 EMS regions and provided categorical funding for the development of specific emergency medical systems, services and facilities. The national Health Planning and Resources Development Act of 1974 increased planning activities and services to assist the states in the development of more comprehensive EMS systems. Today, most states have identified lead agencies that regulate the provision of basic and advanced prehospital care and primary and continuing educational programs. Federal categorical funding for EMS system development ended in the 1980's and was replaced by block grant funding. As a result, funding for EMS since the 1980's has been substantially curtailed.

Since 1966, emergency medical care has been considered transportable. The focus of the EMS effort is to deliver increasingly advanced forms of medical care at the point of incident, rather than delaying advances care until arrival in the hospital setting. It is believed that by extending the capabilities of the emergency department to the scene of the accident or illness, time-to-treatment will be abbreviated, and morbidity and mortality will be effectively reduced.

In support of this assumption, sophisticated system have been developed in the areas of regulation, education, research, standards and technology. Attempts to validate the original assumption have focused more on compliance with established methodology (form) than on scientific findings derived from patient outcomes (function).

Unfortunately, no universal data on the demographics of EMS demand, treatment or provider composition in the U. S. Current estimates of annual, civilian emergency medical responses range upwards of 21,000,000 (not counting interfacility transports). Patient transport percentages vary widely, but average approximately 67 percent (14,000,000). Approximately 33 percent (4,260,000) of these receive some form of advanced life support treatment.[2] EMS transport provider types include fire service, private, hospital based, military, air medical, municipal and county department and volunteer rescue, fee-for-service rescue, special events, law enforcement and authorized off-duty personnel from all categories. The total number of transporting and non-transporting air and ground EMS vehicles among all provider types, as well as the total number of military emergency responses and transports remain unknown.

In the age of health care reform, providers are required to demonstrate the necessity, efficacy and practicality of the health care they deliver, relative to available health care dollars. For years, the health care industry has taken steps to meet this requirement, however, its EMS sub-component has yet to establish even the relative medical effectiveness of advanced life support (ALS) care over basic life support (BLS) care.[3] Moreover, EMS researchers and practitioners have been largely unsuccessful in their attempts to reproduce comparable patient outcomes among geographically disparate EMS systems.

Although numerous outcome-based ALS studies have been conducted over the past 25 years, the stability (identity, strength, quality and purity) of the drugs used in the uncontrolled environment of the prehospital setting was never established, maintained or reported. This omission, which is rooted in the assumption of transportability, represents a critical oversight on the part of the EMS industry - and one which requires immediate and comprehensive reform.

Concern over the de-stabilizing effects of temperature extremes on prehospital drugs was first reported in 1985.[4] The Palmer study found that temperatures encountered in the prehospital setting are far more extreme than those required for safe drug storage. Further, excessive medication temperatures are sustained, disproportionate to their ambient environment. The study did not report the effects of the extreme cold conditions or prehospital exposure to sunlight and humidity. It did suggest that drugs used in the prehospital setting are being chemically altered as a result of the unclimatized storage conditions that are indigenous to the EMS setting.

Subsequent studies reported results that appear to be associated with the length of exposure toe temperature extremes. On study reported an 11 percent loss of parent isoproterenol and changes in the ionized state of epinephrine after four weeks of exposure to extreme heat. [5] Another showed no changes in the drugs tested when subject to 16 hours of variable temperature extremes.[6] No studies conducted to date have attempted to determine the remaining bioactivity in drugs subjected to temperature extremes.

Investigation into the effects of excessive temperatures on drugs is not limited to the United States. In 1991, Hogerzeil, et. al, reported the effect of temperature extremes on a consignment of drugs that was shipped from the Netherlands to the Nile Province Essential Drugs Project in Sudan. They were subsequently transferred to the Central Medical Stores in Khartoum. An analysis of their potency was made and compared to original batch samples. Three of the drugs showed losses potency; Adrenaline (-14.4%), Ergometrine (-

18.4%) and Retinol (-12.5%). The authors concluded that “For Adrenaline and Ergometrine injection this has serious medical consequences...[7] This study followed earlier reports of thermally induced drug degradation in the region.[8]

In 1991, the World Health Organization and UNICEF conducted a study of drug stability during international transport.[9] The study was part of an ongoing effort by the international scientific community to develop and implement administrative controls for the international distribution of pharmaceuticals.[10] In 1993, Hogerzeil, et. al, reported on the stability of Oxytocics in tropical climates.[11] The study concluded that “in only 31 percent of the field samples taken from six tropical countries the level of active ingredient complied with the USP/BP limits of 90-110 percent of the stated content, while 31 percent of the samples contained less than 60 percent.

Northwood reported degradation effects caused by a drug cupboard light that failed to switch off when the door was not fully closed. A thermometer was placed in the cupboard and showed in ambient temperature of 44 degrees Celsius. One of the drugs stored in the cupboard, labetalol, was affected. Northwood stated”at 37 degrees Celsius discoloration of the solution is seen and the active compound id degraded. A poor response to this vasoactive drug could thus be anticipated, which could have serious clinical implications, especially if used in a situation of urgency.” [12] While these international reports are not EMS specific, they reaffirm both the thermal vulnerability of pharmaceuticals and the global nature of this problem.

The efficacy of human drugs and biologist is established and assured by means of highly specific testing and regulatory processes established in the U.S. by Congress and enforced by the Food and Drug Administration (FDA). All domestic and foreign pharmaceutical manufacturers are required to comply. As a result, effective therapeutic concentrations are established and assured. In addition, specific stability testing and continuous monitoring is required to determine expiration dates, handling and storage requirements.[13]

Drug stability is affected by temperature, light. radiation, humidity and other adverse factors. Stability- testing protocols employed by pharmaceutical manufacturers are required to include (where applicable) the measurement and disclosure of: sterility, strength, appearance, color, particulate matter, pH, pyrogenicity, dispersibility, lethality,

bioactivity, odor, homogeneity, resuspendibility, particle size, consistency, clarity, viscosity, dissolution, precipitation, container-closure interaction, moisture, hardness, friability, bioavailabiltiy and bioabsorption. The expiration date marked on each drug's container is valid only when these original properties are assured by strict adherence to the storage conditions specified for each drug.[14] "Individual storage requirements [of all pharmaceuticals] must be observed throughout the distribution of the article, i.e., beyond the time it leaves the manufacturer, up to and including its handling by he dispenser or seller of the article to the consumer." [15]

In the interest of the public health and welfare, the FDA classifies improperly stored drugs as adulterated due to the potential of their adverse therapeutic effects:" A drug or device shall be deemed to be adulterated - (a) (1) if it is a drug and the methods used in, or the facilities or controls used for its manufacture, processing, packing or holding do not conform to or are not operated or administered in conformity with current good manufacturing practice to assure that such drug meets the requirements of this Act as to safety and has the identity and strength, and meets the quality and purity characteristics, which it purports or is represented to possess; or (b) if it purports to be or is represented as a drug the name of which is recognized in an official compendium [USP-NF], and its strength differs from, or its quality of purity falls below, the standard set forth in such compendium."[16]

Implications for EMS

Since the inception of modern emergency medical services systems, the body of knowledge in the practice of emergency medicine has grown rapidly. Scientific evidence was quickly translated into treatment standards and guidelines as it became available. The development of paramedic training and practice saw the introduction and incorporated use of many drugs in the prehospital setting. That is where the original assumption of transportability failed. Drugs were transferred from the stable environment of the hospital setting to the unstable environment of the prehospital setting.

Prehospital drug therapy is based on the use of treatment algorithms that are constructed in a manner to yield positive and negative results to establish the course of prehospital treatment. Logically, these algorithms presume that the drugs used will possess their purported characteristics and will not have been compromised by thermal extremes or other adverse storage conditions.

The vast majority of prehospital drugs are required to be stored at Controlled Room Temperature, which is defined in terms of "25 degrees [Celsius] at the maximum mean kinetic temperature, with allowed excursions between 15 and 30 degrees [Celsius] [59-86

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degrees Fahrenheit]" [17] This new definition was created to ensure "...continuity of storage conditions from product development to dispensing to the patient."
The drugs are manufactured, tested and granted FDA approval based on their stability within that reported stability range. Storage of drugs outside the established range voids the expiration date, which is printed on the drugs' containers or packaging. More importantly, both pharmaceutical manufacturers and the FDA understand that subjecting drugs to thermal conditions outside the required storage range ultimately results in chemical degradation and changes in concentration and bioactivity. Sunlight also affects drug stability. [18]

A common practice among EMS providers is to remove drugs from their original packaging and place them in open holding trays located in their vehicles. This is done to facilitate access while working under emergency conditions. As a result, these drugs are subjected to varying intensities of sunlight (in addition to thermal extremes) and eventually administered to prehospital patients.

The problem of adulterated drugs must be considered in the context of a prehospital treatment algorithm. Some or all of the drugs used are potentially in some state of adulteration and possess something less than their full therapeutic concentration. The treatment pathway could be misdirected, based on negative results obtained from their use. In addition, diagnostic agents, which also require environmental protection, could dictate a course of treatment, or non-treatment, based on false-positive or false-negative finding.

Accordingly, drug calculation using adulterated articles are incorrect. In the course of FDA approval, pharmaceutical manufacturers conduct human trials to establish the effective concentration of each drug. Often, these determinations and subsequent administration criteria are based on the mass of recipient. Furthermore, stability testing requires that precise formulations be determined at the time of testing. At that point, the drugs possess their full therapeutic potential; however, if the drugs possess something less than their original concentration, new administration formulae would be required to yield the same therapeutic results, and new stability testing would be required on the alternate formulations. Because the rate of thermal degradation among drugs is variable, paramedics have no means to determine how much concentration of each drug remains, and how much bioactivity can be expected.

A 1991 study reported the experience of "at least one of the Tennessee paramedical services [as having] consistently noticed a lack of predicted response to cardiac medications, which were not out of date... A lack of positive response to epinephrine was noted during some prehospital cardiac resuscitations, suggesting the temperature extremes as a possible source of drug degradation." The investigators were led to conclude that " drugs rendered unstable by exposure to temperature extremes can create a catastrophic situation of which many ALS providers were unaware... Many of the cardiac drugs are sensitive to temperature extremes, but additional studies should be done to ascertain the magnitude of this problem. " [19]

In a Mississippi statewide survey, “All services reported that drug storage areas in vehicles are climate controlled for temperature extremes at all times. “ Upon verifying investigation, however, the state staff concluded” ...that climate controls for [drug] storage does not [sic] exist.” [20] The State of Mississippi currently has EMS regulations that require providers to adhere to the drug manufacturers’ recommended storage temperatures.
The State of Utah requires greater accountability on the part of local physician advisors and EMS provider organizations. The Utah regulation states, “All medications shall be stored per the manufacturers’ recommendations for temperature control and packaging requirements. A record shall be maintained which records the minimum and maximum temperatures inside each drug box during each 24 -hour period. Any medications known or suspected to have been subjected to temperatures outside the recommended range shall be returned to the hospital for replacement.” [21]

The provision of ALS care in the United State, indeed, the world, is based on the belief that the drugs used in the prehospital setting are, in fact, what they purport to be. EMS physicians and researchers have long been concerned with the reproducibility of clinical outcomes. This suggests that the variable of unclimatized drug storage and the use of adulterated drugs could be of central importance.

The validity of the ALS research to date is questionable because the therapeutic value of the drugs used was neither established nor assured. No determination of clinical effectiveness can be suggested or asserted without first controlling this fundamental variable. Recent trends in ALS care have led to the removal of certain drugs in some EMS systems (i.e., isoproterenol). While found to be efficacious in the hospital setting, theses drugs were found to be less effective when used in the prehospital setting. The change of treatment environment that renders drugs less effective again suggests that adulteration due to climatic conditions may be responsible.

As a matter of operation policy, most paramedics are required to frequently note the expiration date of the drugs they carry. The assumption is that the expiration date guarantees the drugs’ potency. Most EMS medical directors also follow this assumption and either knowingly authorize the administration of adulterated drugs to patients in the field. Unknown to most is the fact that pharmaceutical manufacturers will not warrant their products if they are stored under conditions other those specified on the articles’ container. [22]

Many EMS services and systems have established a policy of exchanging drugs (by agreement) between the prehospital environment and the hospital environment before their believed expiration dates. The expiration dates of these drugs however might no longer assure their efficacy if the drugs have not been properly stored. Therefore, hospitals can become unknowing participants in the administration of adulterated drugs to in-house patients.

The effects of excessive heat and cold on pharmaceutical agents are amply demonstrated; however, the physiologic impact of administering excessively hot or cold agents is generally not considered by prehospital providers . The effects of administering near freezing parenterals – a condition frequently encountered in the EMS environment– appear to be more generally understood in the surgical community. Freezing climactic conditions create problems with viscosity, crystallization and bioabsorption in addition to a wide variety of physiologic manifestations ranging from vasoconstriction to the problems encountered with induced hypothermia. The effects of administering hot parenterals appear to be less widely understood.

Anecdotal reports of creative attempts to thaw and reconstitute frozen parenterals are commonplace. Obviously, frozen drugs cannot be administered to patients, but some rapid re-warming techniques employed by emergency medical technicians (including placing intravenous solutions on the vehicle's engine and pre-filled syringes under the provider's armpits) seem both medically inappropriate and potentially harmful. Regardless of success with these street-thawing techniques, these drugs are considered by law to be adulterated.

A review of the current training materials for EMT's and paramedics revealed no reference to prehospital drug stability nor any consideration for safe drug storage. Despite growing evidence that the scope and magnitude of this problem is increasingly acknowledged, even emergency medicine texts have yet to recognize its gravity.

In the past 20 years, sophisticated operational and clinical quality assurance programs have been developed and integrated to EMS. These programs chronicle, assess and report on virtually every element associated with the provision of emergency medical care; however, they fail to capture pertinent data on the stability of drugs administered in the prehospital setting. This omission appears to negate the validity of prior and subsequent procedural and clinical events. For example, dispatch time, response time and access time
criteria for out-of-hospital cardiac arrest are rendered irrelevant once the patient has been administered adulterated drugs. Likewise, the measurement of on-scene time, transport time and subsequent resuscitative efforts is of little value. None of the events proceeding or following the administration of adulterated drugs should be considered meaningful when analyzing the determinants of successful outcomes from out-of-hospital cardiac arrest.

The costs associated with the provision of EMS continue to spiral upward, driven by a variety of operational factors. Reimbursement for ambulance services has risen at an average annual rate of more than 20 percent since 1974 -- twice the rate of medical inflation. [23] A recent study examining the use of ambulance services under Medicare was completed at the request of the Health Care Financing Administration (HCFA), in response to section 6136 of the Omnibus Budget Reconciliation Act of 1989 (Public Law 101-239). [24] The study reported "disagreement in the literature about the medical effectiveness of ALS services..." This suggests that HCFA, when proposing future protocols that will determine

when ALS services are medically warranted, will place the burden of proof, connecting health care costs to clinical outcomes, on the providers . It is unreasonable to assume that payers of health care will continue to reimburse prehospital providers for the pharmacologic aspects of ALS care unless the stability and efficacy of the drugs they administer can be substantiated and assured by means of strict administrative controls.

The problem arising from the use of adulterated pharmaceuticals is one of benign failure: adulterated drugs cause harm by failing to achieve purported therapeutic effects rather than causing harm due to their administration. Whether analyses are made at autopsy to determine if concentrations of resuscitative drugs exist in sufficient quantities to have been to benefit is unknown. The question, therefore, is not whether drugs administered in the EMS environment are causing fatalities but whether they are failing to prevent fatalities.

No thorough discussion of this issue would be complete without disclosing the profound legal consequences of sub-standard drug storage and the administration of adulterated pharmaceuticals. As discussed in the following section, federal and state laws and regulations provide for criminal and civil penalties (imprisonment and fines) for introducing into commerce any adulterated drug. [25] Common law negligence and the doctrine of strict liability in tort indicate additional liability concerns for providers. These areas of exposure, as well as consumer protection/deceptive trade practices, will be explored as potential litigious concerns for the EMS industry.

II. LEGAL IMPLICATIONS

As discussed in the preceding section, pharmaceuticals carried by emergency medical providers offering advanced life support (ALS) are required to be stored within certain temperature ranges. [26] These required temperature ranges are established either by the drug manufacturer or by regulation. [27] Studies have shown that exposing drugs to temperature extremes can alter the characteristics and quality of drugs. [28] Further, many drug manufacturers will warrant and guarantee their products' quality, potency and characteristics only if their drugs are stored at recommended temperature ranges.[29] This analysis assumes, therefore, that exposing various ALS drugs to temperature extremes (as well as other climatic extremes) alters the inherent quality and/or characteristics of many such drugs.

The issue presented is what potential liability exits for persons in the chain of distribution of drugs utilized by EMS personnel, for administering to patients drugs that do not have the identity or strength, or fail to meet the quality and purity characteristics such drugs purport to or are represented to possess, because such drugs have been exposed to temperature extremes as result of improper storage of such drugs by EMS personnel.

This analysis is limited to a general discussion of potentially applicable theories of liability and does not purport to be an exhaustive review of all existing statutory and common law. Further, no extensive effort has been made to determine the extent to which each state might have altered or limited the application of general theories of liability to certain health care providers. [30] Because of the author's greater familiarity with the laws of the State of Texas, references may be made to specific Texas law for illustrative purposes.

Food, Drug and Cosmetic Acts

The Federal Food, Drug and Cosmetic Act (the "Federal Act") [31] prohibits introducing into interstate commerce any adulterated drug, [32] causing the adulteration of any drug already in interstate commerce, [33] or receiving any adulterated drug and thereafter delivering or

proffering for delivery such drug for pay or otherwise. [34]

The Federal Act provides in pertinent part that a drug is deemed to be adulterated if the methods used in or the facilities or controls used for the drug's manufacture, processing, packing or holding do not conform to or are not operated or administered in conformity with good manufacturing practice to assure that such drug has the identify and strength , and meets the quality and purity characteristics which such drug purports or is represented to possess,[35] or if it is a drug which is recognized in a official compendium and its strength differs from or its quality or purity falls below the standard set forth in such compendium,[36] or if the drug is not recognized in an official compendium and its strength differs from, or its purity or quality falls below, that which it purports or is represented to possess.[37]

The United States Pharmacopoeia ("USP") is an official compendium to these federal regulations.[38] The USP provides in pertinent part that "individual storage requirements [of all pharmaceuticals] must be observed throughout the distribution of the article, i.e., beyond the times it leaved the manufacturer up to and including its handling by the dispenser or seller of the article to the consumer."[39] The USP also provides generally that where recommended storage conditions are stated on the label of a pharmaceutical, one must adhere to those conditions. Absent special instruction, the product should be stored at a temperature range between 15 and 30 degrees Celsius. Effective January 1, 1995, controlled room temperature will be defined as 25 degrees Celsius as the maximum mean kinetic temperature, with allowed excursions between 15 and 30 degrees celsius.[40]

Although no private right of action exists under the Federal Act,[41] any person who dispenses and adulterated drug into interstate commerce can be imprisoned for up to one year or fined up to $1,000 or both.[42] A repeat violator could be imprisoned for up to three years or fined up to $10,000 or both.[43]

Texas Food, Drug and Cosmetic Act

The State of Texas has adopted its own Food, Drug and Cosmetic Act.[44] The Texas Act as does the Federal Act, prohibits introducing into commerce any adultered drug.[45] The Texas Act defines an adulterated drug in essentially the same manner as the Federal Act.[46] Under the Texas Act, a person who dispensed and adulterated drug into commerce commits a class A misdemeanor.[47] Moreover, a person dispensing an adulterated drug into commerce may be assessed a civil penalty of up to $25,000 per day for each violation.[48] Significantly, the Texas Act specifically provides that in a criminal proceeding, to prove intent, knowledge, recklessness, or criminal negligence to establish criminal responsibility for violating the Act is not necessary.[49]

Although the Federal and Texas Acts have traditionally been applied to drug manufacturers and pharmacists, nothing in either Act precludes the Acts' application to EMS providers and the physicians under whose authority they operate. Any EMS personnel who causes or allows a drug to become adulterated because of improper storage of such drug in the field, and thereafter administers such drug to a patient, violates the Federal Act and Texas Act, thereby, becoming subject to the civil and criminal penalties authorized under the Acts. In the Ems context, this could include the physician medical director, EMS field personnel and the operator of the EMS system. Moreover, under the Texas Act, the appropriate governmental attorney is commanded to initiate and prosecute appropriate governmental attorney is commanded to initiate and prosecute appropriate proceedings without delay against a person reported to them to have violated the Texas Act.[50]

Common Law Theories of Negligence

The most common theory of common law liability in the health care field is negligence. To establish negligence, one must prove that the Defendant deviated from accepted standards of conduct by his or her acts or omissions. The traditional elements of negligence are a follows:

(1) a duty or obligation, recognized by law, requiring a certain standard of conduct to protect others from unreasonable risk;
(2) a failure to conform to the required standard, that is a breach of the

duty;
(3) a causal connection between the breach of duty and the injury;
(4) resulting in an actual loss or damage.[51]

The applicable standard of conduct may be prescribed by legislation or regulation.[52] Consequently, the violation of such enactment is tantamount to a breach of the standard of care.[53] A violation of industry custom or standards can also be evidence of negligence.[54] Conversely, proof of a Defendant's compliance with relevant statutes, regulations or industry standards is admissible as evidence of due care.[55]

Proof of the breach of duty or failure to conform to the required standard of care may be established by direct or circumstantial evidence. For example, *res ipsa loquitur* ("the thing speaks for itself") is a theory of inference of negligence which appears applicable to the issue of dispensing drugs which have been improperly stored. Its elements are as follows:

(1) injury would not occur in the absence of negligence;
(2) injury must be caused by an agency [i.e., adulterated drug] within the Defendant's exclusive control; and
(3) injury not caused by the act of the Plaintiff.[56]

With respect to drug storage, the standard of care is well established by law, regulation, industry standards and industry practice. The USP requires storage in accordance with manufacturers' instructions, and if no instructions exist, then at room temperature. Most manufacturers establish the proper storage temperatures for their drugs. Some state regulations require EMS personnel to store drugs properly.[57] More importantly, no health care provider could seriously contend that it is an acceptable practice to dispense drugs which might have diminished efficacy due to improper storage. Accordingly, the only proof necessary to establish breach of duty is possibly to show that a dispenser of drugs has failed to store them within proper temperature ranges. If the remaining elements of negligence can be proven, liability is established.

Strict Liability in Tort

The most common theory of liability in drug product litigation is strict liability in tort. Section 402A of the Restatement (Second) of Torts (1965) provides:

(1) One who sells any product in a defective condition unreasonably dangerous to the user or to his property is subject to liability for physical harm thereby caused to the ultimate user or consumer, or to his property, if
(a) the seller is engaged in the business of selling such product, and
(b) it is expected to and does reach the user or consumer without substantial change in the condition which it is sold.

However, subsequent changes or alterations in the product will not relieve the Defendant from strict liability if the changes were foreseeable and did not unforeseeably render the product unsafe.[58] Under this theory of strict liability, no privity of contract is required; in other words, any consumer is a potential plaintiff.

In recognition that certain products are unavoidably unsafe, yet the benefit of such product outweighs the risk, an exception to strict liability in tort has been developed which applies to drug manufacturers; this is expressed in Comment k to Section 402A. Generally, comment k provides that since the benefit drugs provide outweighs the risk inherent in drug usage, no strict liability exist in tort if the product is properly prepared and marketed and proper warnings are given.[59] Consequently, the only theories of recovery sounding in strict liability against drug manufacturers would be for their failure to warn of known or reasonably knowable defects or other improper or negligent marketing efforts.[60]

Historically, manufacturers have satisfied their duty to warn under the aegis of the "learned intermediary rule" by making appropriate disclosure to the prescribing physician.[61] The adequacy of the warning, however, is determined by the negligence standard.[62] This can result in the complete shift of liability to the physician.[63] This warning typically takes the form of a package insert, which can also establish a standard of care for negligence purposes.[64]

Once a drug manufacturer knows or should know that its drug is being stored outside recommended temperature ranges, thereby potentially resulting in the administration of this drug in an altered state, its duty to warn and its methods of marketing drugs might change dramatically. Drug manufacturers must exercise the reasonable care and skill of experts in the pharmaceutical industry in the design, development, testing, marketing and follow-up surveillance of their drugs (emphasis added).[65]

By benefit of adequate warning the pharmaceutical company's duty can be discharged and liability shifted to the treating physician. The physician has the duty to prescribe drugs with the appropriate therapeutic effect.[66] To prescribe drugs which have lost their efficacy or have altered qualities or characteristics because of exposure to temperature extremes might well constitute a breach of this duty. Conversely, a physician who prescribes a drug in full conformity with manufacturers' recommendations is generally thereby relieved of liability for injuries caused by the drug.[67]

In the EMS context, emergency medical technicians and paramedics generally operate under the direct supervision and instruction of a physician. Directly or indirectly, the physician orders the administration of the drug. If the drug is adulterated, such physician has liability as the "treating physician."

Breach of Warranty

Other possible theories of liability exist under contractual theories, such as for breach of express or implied warranties. These theories age governed by the Uniform Commercial Code, which has been adopted in some form by all states except Louisiana.

Express warranties are created as follows: (i) any affirmation of fact or promise made by the seller to the buyer which relates to the goods and becomes part of the basis of the bargain, creates and express warranty that the good shall conform to the affirmation or promise, or (ii) any description of the goods which is made part of the basis of the bargain creates an express warranty that the goods shall conform to the description.[68]

The implied warranty of merchantability[69] means generally that the goods:

(1) pass without objection to the trade under the contract description; and
(2) in the case of fungible goods, are of fair average quality within the description; and
(3) are fit for the ordinary purposes for which such goods are used; and
(4) run, within the variations permitted by the agreement, of even kind, quality, and quantity within each unit and among all units involved; and
(5) are adequately contained, packaged, and labeled as the agreement may require;and
(6) conform to the promises of affirmations of fact made on the container or label if any.

The implied warranty of fitness for a particular purpose means that when the seller knows that the buyer is relaying on the seller to select of furnish suitable goods for the buyer's particular purpose, the implication is that the goods so selected shall be fit for such

purpose.[70]

These theories are not commonly utilized in the health care context because several legal hurdles and limitations must be overcome. Privity of contract is often an issue;[71] damages can be modified or modified or limited; and the warranties can be disclaimed or limited. Some states have statutorily limited the use of these theories in the health care arena.[72] Despite these hurdles, under appropriate circumstances, these theories might apply.

Consumer Protection Acts

Many states have consumer protection legislation which has potential application for the issue of proper drug storage. The Texas statute has been asserted as a basis for liability in the EMS context.[73] The statute provides that it is an deceptive act or practice to represent goods or services as having characteristics...[or] benefits...which they do not have.[74] [75] Further, under the Act, a consumer can maintain a cause of action for any deceptive act or practice or for breach of an express or implied warranty.[76] Although this legislation was obviously designed for application in the commercial context, creative plaintiffs might successfully argue its application in the health care industry.

In conclusion, a myriad of laws with application to persons in the chain of distribution of drugs can impose liability for administering adulterated drugs;

- The EMS physician, technician and operator are all subject to civil and criminal penalties for violations of applicable Food and Drug and Cosmetics Acts, regardless of whether injury to any person occurs. The manufacturer and pharmacist who know adulterated drugs are being dispensed might also have exposure;

- The manufacturer who knows or should know that its drugs are being improperly stored has the duty to warn about the misuse and possibly the duty to protect the drug in the marketplace. The breaches of these duties can result in strict liability under the theory of negligence, and might violate applicable federal regulations;

- The EMS physician has the greatest exposure under theories of negligence and strict liability in tort. As the learned intermediary, he can inherit the drug

manufacturer's liability. As a medical practitioner, he must adhere to applicable standards of care. These standards are easily established. Moreover, he has potential liability for all persons acting under his direction and authority;

- The emergency medical technician and paramedic have liability under theories of negligence and possibly strict liability in tort;[77]

- The liability of EMS provider organizations rests primarily in negligence, but because privity of contract may exist vis-a-vis the patient, liability might also be under breach of warranty theories and consumer protection legislation. Federal, state and local laws can subject the provider to civil and criminal liability. Finally, the dispensation of adulterated drugs might constitute a breach of the providers' agreement with the community served;

- The state regulator might also have a duty to prevent known violations of law. Although governmental immunity can be an issue, many states do not protect their officials from negligent behavior.[78]

The absence of reported cases where a patient's injury was directly linked to the administration of an adulterated drug may have allowed this problem to go unrecognized. Injury in all likelihood has occurred; however, the benign or anonymous nature of a drug's simply not working rather than causing an overt reaction, may have allowed the causal connection between administration of adulterated drugs and injury to the patient to be overlooked. Regardless, if injury is merely theoretically possible, it is foreseeable and liability attaches. A more explosive scenario can be created if the problem is recognized but consciously ignored.

An open awareness of this public health problem will necessitate action. Health regulators will be required to enforce existing laws and adopt new ones to address the issues squarely. Drug manufacturers will have to review the adequacy of their warnings and marketing materials. Physicians will have to take care to follow manufacturers instructions and administer only drug which have been properly stored. EMT's, paramedics and provider organizations must store their pharmaceuticals in strict conformity with law, regulation and manufacturers' recommendations. Finally, to ensure compliance with safe and proper storage procedures and to protect health care providers from liability, accurate data and record keeping of compliance must be generated and archived for future reference.

III. MISSISSIPPI ANALYSIS: ACCESS, CONTROL AND STORAGE OF MEDICATIONS

The Division of Emergency Medical Services (DEMS), Mississippi State Department of Health, is the statutorily designated lead agency for the Emergency Medical Services program in Mississippi. Authority for developing the EMS program was rendered in 1974 by the Mississippi State Legislature's passage of the Mississippi EMS Act.[79] As a result of that law and subsequent amendments, DEMS has adopted rules and regulations for a comprehensive EMS program, including pertinent standards for the provision of ambulance service, EMS personnel and equipment. Specific rules and regulations address licensure standards for basic and advanced life support prehospital providers.

In 1993, DEMS published its latest revisions of the rules and regulations manual.[80] New standards regulating access, control and storage of prescription drugs and controlled substances were included.

In an effort to determine the status of advanced life support (ALS) providers with regard to compliance with these standards, DEMS conducted an on-site drug survey with all ALS providers. This reports details the findings of that survey and other research efforts made by DEMS.

Mississippi EMS System

The Mississippi Emergency Medical Services (EMS) system officially began on July 8, 1974, the effective date of the Mississippi Emergency Medical Services Act.

The law charged the State Department of Health with implementation of the Act and outlined specific responsibilities:

- regulation and inspection of public and private ambulance services;
- inspection and issuance of permits for ambulance vehicles;
- training and certification of EMS personnel including drivers and attendants;
- development and maintenance of statewide EMS records program;
- development and adoption of EMS rules and regulation; and
- coordination of an EMS communications system.

The Department established its Division of Emergency Medical Services (DEMS) that same year. Today, DEMS is a viable program of the Mississippi State Department of Health. Working with two major advisory groups, the EMS Advisory Council and the Committee on Medical Direction, Training and Quality Assurance, DEMS had developed a comprehensive prehospital EMS program with rules and regulations patterned after model

national standards.[81]

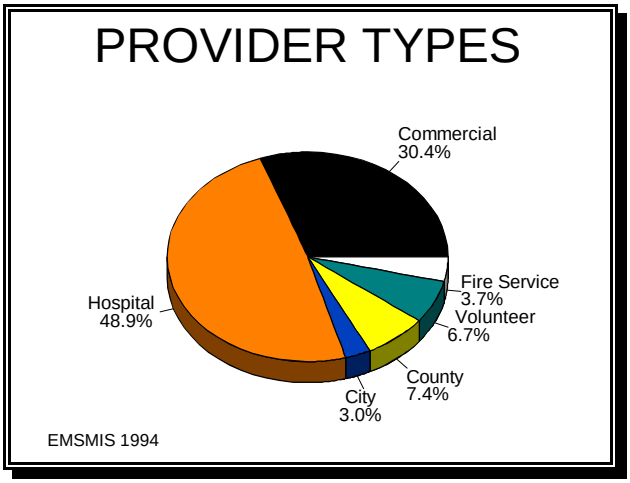

Figure 1

Mississippi has 132 in-state licensed ambulance transportation provider services and four out-of-state providers. DEMS categorizes ambulance service providers into six types; hospital, commercial, fire service, county, city, and volunteer. (See Figure 1) Hospital based ambulance services make up **48.9 percent** of the total prehospital transportation system.

The transportation system in Mississippi conforms to all applicable national standards for design, construction and equipment. The system consists of 433 vehicles ground and air permitted by DEMS. Some **61.7 percent** of Mississippi's population has access to ALS level service, provided by 298 vehicles, while the remaining 38.3 percent receive basic life support (BLS) level service provided by 135 vehicles. ALS level services are those that are staffed and equipped to deliver prehospital care at the EMT-Intermediate or EMT-Paramedic level. BLS level services are those that are staffed and equipped at the EMT-Basic level.

Skill levels of each of the three EMT levels are as follows:

> EMT-Basic with skills in: fracture immobilization, bleeding and wound management, CPR, other basic airway skills, MAST, light extrication.
>
> EMT-Intermediate all skills of EMT-Basic, Advanced Airway Management, (EOA), defibrillation, IV therapy.
>
> EMT-Paramedic all skills of EMT-Basic and EMT-Intermediate, intubation, drug administration (limited), cardiac monitoring, extended optional skills (medical control).

While rules and regulations cover a number of additional service procedural areas for all levels of EMT's and providers, some rules and regulations are specific to ALS. Appendix A is an excerpt of Mississippi rules and regulations which address drug associated standards which are pertinent to this report.

Although Mississippi EMS rules and regulations address specific requirements for ALS prescription drugs and controlled substances with regard to access, control and storage, DEMS does little to measure compliance. And exception is that DEMS staff inspect availability and expiration of drugs required for ALS services four times a year. Other

procedures to verify compliance with access, control and storage, however, presently do not exist.

A serious problem involves the EMS regulation governing the storage of drugs within temperature ranges recommended by the manufacturer. DEMS has never routinely monitored provider attempts to comply with this standard. Rather, staff have assumed that ALS services are cognizant of these regulations and required temperature ranges and have implemented appropriate local policies and procedures to adequately address the federal laws and the DEMS regulations. They also have assumed that physician medical directors, because of physician responsibilities established by law and potential civil/criminal penalties, were aware of this issue and were taking appropriate precautions to comply with these drug laws and other federal/state regulations.

Data collected in calendar years 1992 and 1993, indicate an unexpectedly low rate of administration of prehospital drugs by ALS personnel. (See Figure 2) Mississippi regulation allows 25 different drug items (excluding IV solutions) to be available on all ALS responses. The rate of use during 1992 and 1993 shows that a major portion of these drugs and IV solutions are subjected to extended periods of substandard temperature storage before use, if used at all.

During calendar year 1993, Mississippi EMS providers responded to 251,624 calls. Of these responses 150,834 runs were made by services capable of providing care at least at the EMT-Intermediate and/or the EMT-Paramedic levels. Sixteen percent of those responses included some type of IV administration, while drugs were given to only six percent of all patients treated. Similar rates were documented for calendar year 1993 in Tennessee.[82]

The rates of utilization for calendar year 1992 were virtually the same. ALS capable personnel made 128,583 of 226, 043 total calls. Sixteen percent of these calls included IV therapy while six percent included drug administration. (Figures 2 and 3.)

These low usage rates, documented for two calendar years, indicate that previously published adulteration drug studies fall very short of actual lengths of substandard temperature exposure found in Mississippi. (Figure 4.)

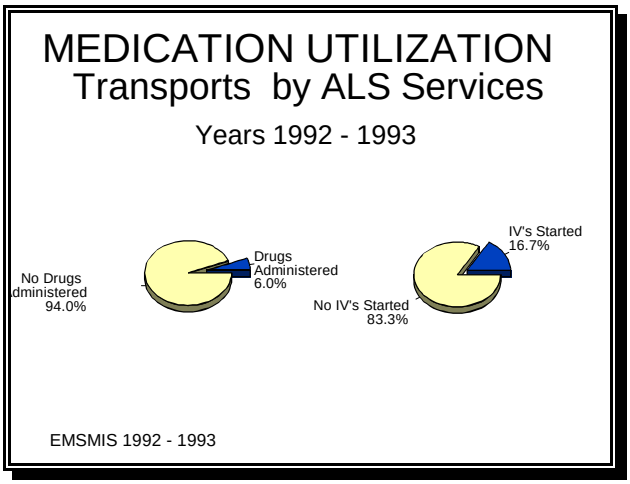

Figure 2

In Mississippi the DEMS has determined that it is the rule rather than the exception that ALS services carry two rounds of drugs on every call. This often does not reflect extra dosages carried by crews and/or kept in permanent supply on board many ALS vehicles, thereby compounding many times the lengths of substandard temperature exposure created by nonuse. Any number of statistical comparisons can be developed which might emphasize further the extended temperature exposure time. For instance, Aminophylline, was used 21 times in 1992 by Mississippi ALS services. Given that 298 ALS vehicles operating in Mississippi carry two doses of each drug required, one might conclude as follows: 288 x 2 = 596 doses - 21 used = 575 unused for one calendar year. At this rate, 27.4 years would be required to use the additional 575 doses carried by ALS providers. Admittedly, expiration dates would affect this extraordinary conclusion, which underscores however, that drugs are carried for extreme periods of time without usage.

MEDICATION UTILIZATION

Years 1992 - 1993

	'92	'93
Total Runs	226,043	251,624
Total Transports by ALS	128,583	150,834
IV's Started	20,809	24,676
Drugs Administered	7,634	8,614

EMSMIS 1992 - 1993

Figure 3

To determine the status of Mississippi ALS providers' compliance with these laws and regulations , DEMS designed a questionnaire which addressed drug access, control, storage and record keeping systems throughout the state.

The 11-page questionnaire consisted of three sections: IV Fluids, Medications and Controlled Substances. Each section contained similar questions about methods of obtaining items, authority, bulk storage, storage after dispensing to EMS units and/or personnel, security, access climate controls and record keeping. The DEMS team conducting the survey recorded answers to each question. After each interview and site visit, all three teams reviewed each survey for accuracy and comprehensiveness. After all ALS provider sites had been reviewed, the team members consolidated survey results into the final report.

MEDICATION USAGE

Years 1992 - 1993

Medications Used	'92	'93
Atropine	1,414	1,437
Aminophylline	21	24
Bretylol	27	30
Bronchodilator	696	950
Decadron	37	35
Dextrose 50%	972	1,006
Demerol	92	128
Diazepam	242	287
Epi. (1:1,000)	85	118
Epi. (1:10,000)	1,500	1,484
Furosemide	458	480
Isuprel	11	12
Lidocaine	702	753
Mannitol	7	5
Morphine	439	413
Naloxone	382	336
Nifedipine	157	296
Nitroglycerine	2,101	2,343
Nitrous Oxide	4	5
Oxytocin	5	6
Procainamide	6	3
Vasopressor	25	44
Verapamil	21	11
Sodium Bicarbonate	322	305
Thiamine	68	76
Other	902	1,147
No Medication Administered	121,078	141,825

EMSMIS 1992 - 1993

Figure 4

because of the questionnaire's construction ,repetitive findings show consistency in 17 significant areas:

1) Over 90 percent of Mississippi ambulance services licensed at the EMT-Intermediate or EMT-Paramedic level obtain IV fluids and other medications (prescription drugs and controlled substances) from hospital facilities i.e. central supply, pharmacy. The remainder obtain these medications from drug companies. Usually, these medications are ordered via purchase orders and/or requisitions.

2) Through formal agreements, service managers, medical directors, emergency room nurses and pharmacies provide authority for ambulance services to obtain medications.

3) Pharmacies and internal pharmaceutical store rooms normally provide bulk storage for hospital-based ambulance services. Primary business locations and vehicles provide storage for the others. Hospital-based services have better access to

climate controlled bulk storage than do other services. Although other non-hospital based service reported bulk storage facilities to be climate controlled, DEMS staff noted that storage usually is related to where the working EMT and vehicle are located and cannot be considered climate controlled.

Ambulance personnel think security for bulk storage is adequate, but DEMS staff discovered that security relates to access by the general public, not employees. DEMS noted that ambulance services staff, including managers, medical directors, and EMT's have access to bulk storage areas.

4) Medications and IV fluids distribution from bulk storage facilities to ambulance services personnel varied, with IV solutions are dispensed more liberally. Service managers generally assigned prescription drugs to vehicles and/or personnel for their drug/response kits. Request from staff or other types of exchange systems replenish the supplies. DEMS staff noted that although these assignments are made by management, they are made very liberally. The service's medical director or medical authorities usually assign controlled substances. Again, DEMS staff noted a very liberal attitude by service management and medical directors regarding the allocation of controlled substances and their replacement. Record keeping systems consist of requisitions, ambulance run sheets, physician prescriptions, charge slips, bills and a range of other inventory control methods. Records for IV solutions are treated very loosely, with minimal, if any, records. Prescription drugs and controlled substances records are questionable in that little verification is done by management or medical control authorities to verify use of drugs for replacement. While a few services do have rigid controls regarding controlled substances, most do not.

5) Services throughly check expiration dates, packaging and medications for expiration dates, leaching and general condition. Of all of the processes reviewed in this survey, this seem to be the most thorough.

6) IV solutions are stocked on vehicles, not removed unless used, and are openly available to ambulance service staff. Through requisition and exchange systems prescription drugs are stocked on vehicles and/or response kits; some services use storage containers which are sealed until use and are resealed after drugs are restocked. A pharmacy or use exchange system generally provides controlled substances.

7) After distribution to personnel, IV solutions and prescription drugs are usually stored on the ambulance vehicle and in response kits. Employees carry controlled substances on vehicles in response kits.

8) The disposition process for expired and partially used IV solutions is liberal. This ranges from flushing unused solutions to discarding in garbage containers. Some ambulance services dispose of prescription drugs via a witnesses process or return them to the dispensary. DEMS noted that the most services simply throw prescription drugs away. Generally, services witness controlled substances' disposal or return them to the pharmacy for disposal or use.

9) Record keeping processes for administration of controlled substances consists of run reports, ambulance service logs, pharmacy forms and combinations. Records for wasting these medications usually are formal documents accompanied by witnessed disposal.

10) Controlled substances usually remain with the vehicle when personnel changes are made. DEMS noted that a few services allow employees to retain these drugs while off duty and claim to make these individual employees personally responsible for drug security. Other common storage is placement within staff lockers. Regarding access, DEMS staff concluded that non-hospital based services have more liberal access policies. Mainly, management conducts random checks to assure that drugs are in fact stored as claimed.

11) Usually the medical director has delegated access to storage of controlled substances to ambulance service management and on duty ALS personnel. DEMS staff noted a very loose approach to this delegation process.

12) DEMS staff discovered that physician verification of orders given for the administration of prescription drugs and controlled substances generally does not exist. However, personnel interviewed claimed verification by monthly quality assurance reviews and other chart audits

13) Controlled substance registration certificates are generally kept in the medical director's office or ambulance service management facility.

14) All services claim drug storage areas in vehicles to be climate controlled, DEMS discovered however, that storage temperature on vehicles and in response kits reflect the vehicle’s location. DEMS staff concludes that climate controls for storage on vehicles does not exist.

15) Ambulance service personnel reported that during the summer months temperature-sensitive drugs are usually left on vehicles or in response kits which may be carried in and out of service operation centers. Some personnel indicated that minimal efforts were made to "shade" the vehicle from sunlight by parking under roofs (bays), trees or with doors and windows left open. During winter months, ceramic heaters, periodic cranking of the vehicle and IV warmers are methods used to protect temperature sensitive drugs. DEMS records show several personnel stated "if our IV's and medications freeze, we don't use them."

16) Most ambulance personnel interviewed stated they do not carry response kits, ALS supplies, drugs and equipment in private vehicles. Some services claim that this is permitted by "a gentleman's agreement" with off-duty staff. DEMS noted that medical control plans filed as part of ambulance service licensure generally do not speak to response by off-duty personnel. DEMS did note, however, that a significant number of EMT's proudly attest to "their private ALS treatment kits" and their ability to respond while off duty.

17) Most ambulance services have company policy that relates to employee drug abuse. DEMS noted that about 20 percent do not have these policies.

Regarding the issue of climate control storage and given the underlying public health theme of safe and legal drug administration, DEMS concluded that no such controls were in place at the time of the survey. **Although some services attempted to control the temperature ranges of their drugs, DEMS found these efforts to be unsuccessful and grossly inadequate.**

Mississippi DEMS informally contacted many other state EMS offices regarding this issue and found it, for the most part, to be of little concern. Two exceptions were the states of Utah and Tennessee.

The Utah Department of Health, Bureau of EMS, reported the adoption of storage regulations in 1986.[83] Although Utah's EMS program reported that area EMS inspectors routinely check ambulance service providers for compliance,[84] Utah EMS providers reported that the issue had been deprioritized by service providers,[85] citing the lack of methodologies which could assure compliance, and the failure of Utah's EMS agency to enforce the related regulations as primary reasons. However, the director of Utah's EMS program stated that approval was granted during inspections "if state service providers attempted to maintain drugs at appropriate temperatures. By the use of insulated containers or otherwise".[86]

The Tennessee EMS agency reported that the issue had surfaced several times over recent years but had never been addressed through the adoption of related EMS regulations.[87] However, a former Tennessee EMS medical director had been concerned about the issue and had advocated regulations which would require ambulance and other EMS vehicles to be sheltered in garages or ambulance bays.[88] These recommendations failed to be adopted by the Tennessee EMS program.

DEMS found no effort by any other states to comprehensively address these issues, particularly temperature controlled storage of IV solutions and drugs.

The FDA and Pharmaceutical Companies

DEMS staff contacted the Mississippi State Department of Health's Director of Pharmacy to

obtain information on inappropriate storage of drugs and the potential impact the administration of drugs that had been inappropriately stored might have on patients receiving such medications. DEMS was directed to contact the FDA and to review the contraindications published by individual drug manufacturers. Specific FDA statutes pertain to this issue. DEMS found however, that these statutes were created before the formal development of EMS systems; therefore, EMS does not appear in the language of the statutes. EMS system personnel are covered by function rather than by specific reference. Violations potentially could result in fines and terms of imprisonment as is discussed thoroughly in the legal review presented in this paper.

The DEMS director formally contacted all drug companies selling or manufacturing drugs required of Mississippi-licensed ALS services. Eighty percent of 22 companies contacted responded with specific information regarding storage and contraindications if not stored properly.

In summary, the drug manufacturers recommend strict adherence to the temperature ranges printed on all product materials and disclaim any responsibility for reactions resulting from improperly stored medications. DEMS could not ascertain if any scientific studies have been conducted by any of the manufacturers regarding the effects of improper storage (as documented in Mississippi) might have on medications and subsequent effects or lack of effects these altered medications might have in patient outcome.

Temperature Study

DEMS focused a controlled temperature study during August, 1993, on placement of drugs within a Type II ambulance training vehicle located at the DEMS office. This ambulance (1988 Ford) was not used or moved during the temperature study. Thermometers (mercury), commonly used by health department staff, were secured outside, above the passenger door window; inside on the second shelf of the ALS cabinet (noted normal inside storage location for on-board IV and drug supplies); and in a commonly used Nylon soft pack, which contained a supply of medications as required by the Mississippi EMS program. DEMS staff recorded hourly temperatures outside and inside of the vehicle as well as inside the drug kit from 8 a. m. till 5 p. m. for five days. The readings showed a significant variance in temperatures outside and inside of the vehicle. (Figure 5). This variance consistently subjected the drugs to a wide range of temperatures, some of which were well beyond the drug manufacturer's temperature storage range.

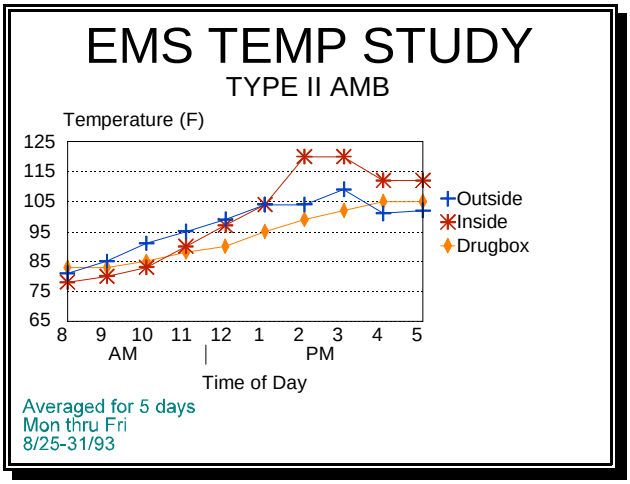

Figure 5

A similar study was conducted during January, February, March, 1994. This study recorded during routine vehicle inspection the temperatures outside and inside of vehicles licensed to ALS services throughout the state of Mississippi. As found in the controlled study, drug storage temperatures were directly affected by vehicle use, vehicle sheltering,

verses other climate conditions. A wide range of temperatures were recorded and again demonstrated that drugs are subjected daily to significant variations in temperature exposure.

Market Search

At the time the targeted issues were developing into significant concerns of the DEMS staff, little was known about the availability of climate-controlled storage equipment other than commercially available IV warmers. A quick scan of the EMS equipment supplier market showed little from which to choose. DEMS became concerned that regulations with which providers cannot possibly comply had been passed.

DEMS searched the EMS market for devices which addressed the storage of medications carried by EMS services and personnel. This market search included a review of all related EMS equipment magazines and other publications. Of the three devices available for purchase, two produced heat or cold by AC or battery power and the third heated solutions by non-electric means. The first of these products is a modification of commonly used fishing tackle boxes which the manufacturer claims maintains medications at a temperature between 60° F and 85° F. This product appears designed to heat, but additional insulating systems offered are designed to help protect medications and solutions from excessive heart in warm weather. The second product investigated uses a commonly available ice chest which, according to the company marketing the product, can "cool to approximately 40° F (5° C) below surrounding ambient temperature or heat to approximately 140° F (60° C). These units cannot be set or regulated to provide for any other temperatures in between the noted hot or cold temperature ranges." The final product investigated is one designed to heat, but apparently not cool, IV solutions to "approximate body temperature in any situation or climate: by non-electric means.

Additional attempts to solve this problem were discovered in fire departments located in Yuma, Arizona and Salt Lake City, Utah.[89] These attempts were primarily efforts to cool storage compartments or to insulate drugs from excessive heat discovered in vehicles utilized by these fire departments. Heating is accomplished through rather basic methods, such as by utilizing a light bulb.

None of the devices investigated seems capable of guarantying consistent temperature controlled storage of medications within the manufacturer's recommended range. None of these devices appear to have the capability of creating a record of internal storage temperatures of warning of temperature violations. DEMS is aware of a patented microprocessor-based product under development which, according to its manufacturer, is capable of maintaining an internal storage temperature within manufacturer's, recommended ranges. This product also purports to have temperature monitoring features, alarm devices activated as prescribed temperature ranges are exceeded, and record keeping and reportability functions which produce a written record of the internal storage temperature at all times. The manufacturer of this product says it will be available in the market place in the first calendar quarter of 1995.

In summary, Mississippi, like most other states, has and EMS regulatory program.

Standards require ambulance services that offer advances prehospital care to carry certain medications believed to be beneficial to certain patients. Mississippi and Utah adopted regulations which address the storage of medications within the recommended temperature ranges of the manufacturers. Some other state EMS directors and medical directors acknowledge concern about this issue, but have not adopted similar standards.

Advanced life support services in Mississippi and possibly throughout the country do not meet the standards required by drug manufacturers regarding storage temperatures. DEMS has additional concerns that these same drugs may be compromised during shipment prior to receipt by licensed EMS services. Additionally, unused drugs inappropriately stored are often routinely rotated (provided shelf life remains current) back into hospital pharmacies for use with other inhouse patients.

Additional federal and state regulations are needed which comprehensively address access, control, storage and record keeping by prehospital healthcare services and personnel. Because some state pharmacy acts identify everyone in the chain of drug distribution as having specific responsibilities for the legal storage of these drugs, including by function but not by name EMS personnel, state-lead EMS agencies need to pursue the connection of EMS laws and regulations to the laws and regulations that govern the practice of pharmacy. Given the obvious responsibility to protect the public health, EMS lead agencies throughout the US and other countries need to collectively address the issue of medication requirements versus access, storage, utilization and record keeping. These agencies should assume the responsibility for the management of data through statewide reporting which assures the appropriate and legal storage of the drugs provided by licensed EMS services and other responder support groups. These agencies need strict administrative controls to accomplish this task.

DEMS seriously questions previously-published ALS efficacy studies and the validity of those studies given the evidence that most drugs administered by prehospital EMS personnel have been inappropriately stored and possibly have been significantly altered by such storage. DEMS suggests that one reason these studies have reach different conclusions may be due to this fact, as stability at the time of administration has never been documented as an issue. Likewise, prior adulteration studies fall short of the actual lengths of substandard temperature and other climatic exposures. DEMS encourages all EMS lead agencies to conduct similar statewide studies and assessments. Further, DEMS suggests that this information should be made available for the collective use in future adulteration studies.

Given the extreme temperature ranges existing in EMS systems throughout the world and the potential impact this could have upon patients receiving these medications, DEMS encourages the FDA to amend its statutes to extend into the prehospital care arena. Other appropriate federal agencies, state EMS lead agencies and other EMS support groups should address this issue through law, regulations and research.

IV. RECOMMENDATIONS

State EMS lead agencies must advise their constituencies regarding this issue and amend their existing EMS rules and regulations to incorporate requirements for the legal and safe storage of pharmaceuticals used in the EMS setting.

EMS physicians must inform their provider organizations, EMT's and paramedics of these findings and require strict administrative controls to ensure the legal and safe storage of prehospital pharmaceuticals.

Educational publications and training curricula must be amended to include the essential elements regarding the legal and safe storage of prehospital pharmaceuticals.

State EMS lead agencies must work to link their ALS related EMS rules and regulations with existing statutes regarding the practice of pharmacy.

Quality assurance programs at the national, state and local levels must be upgraded to incorporate data that will establish that the pharmaceuticals used in the EMS setting are being legally and safely stored, and that climatic and temperature variables have been effectively controlled.

Provider organizations must ensure that EMS drugs are being legally and safely stored, and must implement formal systems of accountability.

EMS researchers must control the variable of drug adulteration in current and future ALS research.

National EMS and Public Health organizations must promulgate public health policies that will accelerate the resolution of this problem.

State EMS lead agencies must establish a formal ongoing means to acquire, archive and manage pertinent data to ensure that prehospital drugs are being legally and safely stored.

The FDA and federal EMS support agencies must extend existing federal drug storage laws to include the EMS industry.

REFERENCES

1. "Accidental Death and Disability: the Neglected Disease of Modern Society", National Research Council, National Academy of Sciences, 1966.

2. "200 Cities Database." Geoffrey A. Cady; JEMS Communications, Inc., Carlsbad, CA, September, 1994.

3. Report to Congress: " A Study of Payments for Ambulance Services Under Medicare," Donna E. Shalala, Secretary of Health and Human Services; p.11; January, 1994.

4. RG Palmer, J Zimmermann, PC Brown, et. al, "Alter States: The Influence of Temperature on Prehospital Drugs." Journal of Emergency Medical Services 10 (1985): 29 31

5. TD Valenzuela, EA Criss, WM Hammergren, et. al, "Thermal Stability of Prehospital Medications, " Annals Journal of Emergency Medicine 18 (1989): 173-176.

6. RB Johansen, NC Shafer, PI Brown, "Effect of Extreme Temperatures on Drugs for Prehospital ACLS, " American Journal of Emergency Medicine 11.5 (1993):450-452.

7. HV Hogerzeil, MJ de Goeje, IO Abu-Reid, " Stability of Essential Drugs in Sudan." Lancet 338 (1991): 754-755.

8. IO Abu-Reid, SA El-Samani, AJ Hag Omer, "Stability of Essential Drugs in the Tropics: A Study in Sudan." Int, Pharm.J 4 (1990): 6-10.

9. HV Hogerzeil, A. Battersby, V Srdanovic, et. al, WHO/UNICEF study on stability of drugs during international transport, WHO/DAP 91.2 Geneva: World Health Organization, 1991.

10. WHO Expert Committee on Specifications for Pharmaceutical Preparations: Thirty-Second Report, WHO Technical Report Series 823, Geneva: World Health Organizations.

11. HV Hogerzeil, GJA Walker, and MJ de Goeje, "Stability of Injectable Oxytocics in Tropical Climates." WHO/DAP 93.6 Geneva: World Health Organization, 1993.

12. D. Northwood, "Temperature and Drug Potency," Anesthesia: Journal of the Association of Anesthetist of Great Britian and Ireland 46 (1991): 11

13. 21 CFR 10.90: Guidelines for Submitting Documentation for the Stability of Human Drugs and Biologics, Office of Drug Research and Review, Center for Drugs and Biologics, Food and Drug Administration, U.S. Department of Health and Human Services, 1987.

14. "Adequate stability data acquired by the manufacturer should be available to support the expiration date and storage conditions specified." United States Pharmacopeia-National Formulary (USP-NF); 23 Ed. 1995, Ch. 1151.
15. USP-NF; 23rd Ed. 1995, chapter 1151

16. 21 USCA; 351

17. USP-NF; 23rd Ed. 1995, lv.

18. Stability Considerations in Dispensing Practice. USP-NF; 23rd Ed. 1995, Ch. 1191:p. 1957.

19. L. Massingale, D. Manis, G. Messor, "Survey of Emergency Medical Services in Tennessee." Journal of the Tennessee Medical Association 48.11 (1991); 535-541.

20. Wade N. Spruill, Jr., Director, Division of Emergency Medical Services, Mississippi State Department of Health, "Access, Control and Storage of IV Solutions, Prescription Drugs and Controlled Substances: A Report on Mississippi Providers of Prehospital Advanced Life Support", 1994.

21. Utah Administrative Rules, R426-3, Section 2.1.4.3.1., Utah Department of Health, Bureau of EMS, January 1994 edition.

22. Compendium of responses from manufacturers of pharmaceuticals. Division of Emergency Medical Services, Mississippi State Department of Health, 1993.

23. Office of the Inspector General (OIG) of the United States, 1987.

24. Project Hope, Center for Health Affairs; Chevy Chase, MD No. 99-c-99168/3-02, October, 1991.

25. 21 USCA; 301

26. For example, the City of Philadelphia Fire Department carries Adenosine, Atropine Sulfate, Bretylium, Diazepam, Dopamine HCL, Epinephrine 1:10,000, Epinephrine 1:1000 and Lidocaine, among other drugs. Each manufacturer of the listed drugs recommends storage at 15-30 degrees Celsius.

27. See generally, United States Pharmacopoeia-National Formulary, 23rd Ed., 1995.

28. RG Palmer, J Zimmerman, PC Brown, et. al, "Altered States: The Influence of Temperature on Prehospital Drugs, " Journal of Emergency Medical Services 10 (1985): 29-31.

29. For example, Parke-Davis, in an unpublished letter dated April 2, 1993, to Wade N.

Spruill, Jr., with respect to their product Nitrostat (trademark), stated: “Potency is only guaranteed if product is stored according to package labeling.” Their package labeling recommends storage at controlled room temperature, 15-30 degrees Celsius.

30. See, for example, Texas Health and Safety code, Vol 5, Section 773,009, which provides: “A person who authorizes, sponsors, supports, finances or supervises the function or emergency room personnel and emergency medical services personnel is not liable for civil damages for an act or omission connected with training emergency medical services personnel or with services or treatment given to a patient or potential patient by emergency medical services personnel if the training, services, or treatment is performed in accordance with the standard or ordinary car.”

31. 21 USCA, Section 301 et seq.

32. 21 USCA, Section 331(a).

33. 21 USCA, Section 331 (b).

34. USCA Section 331 (c).

35. 21 USCA, Section 351(a)(2)(b).

36. 21 USCA, Section 351(b).

37. 21 USCA, Section 351 (c).

38. 21 USCA, Section 321 (j).

39. Supra, note 27.

40. Supra, note 27.

41. See e. g., Brinkman v Shirley, 732 F. Supp (M dist. Pa. 1989) 33, aff’d, 902 F.2d. 1558

42. Supra, note 6, 21 USCA Section 333 (a)(1).

43. 21 USCA. Section 333(2).

44. Texas Food, Drug and Cosmetic Act, Texas Health and Safety Code, Vol. 3, Title 6, Chapter 431 (“Texas Act”).

45. Texas Act, Section 431.021.

46. Texas Act, Section 431.111.

47. Texas Act, Section 431.059.

48. Texas Act, Section 431.0585.

49. Texas Act, Section 431.059.

50. Texas Act, Section, 431.060.

51. W. Keeton, Prosser and Keeton on the Law of Torts, 5th, 1984 ed.: 164-65.

52. Restatement (Second) of Torts, Section 285 (1965).

53. Dixon, Section 10.03[3]

54. Dixon, Section 10.03[3].

55. Dixon, Section 10.03[4]

56. Dixon and Woodside, Drug Product Liability, Vol. 2, Section 10.03[2], Matthew Bender (1994) ("Dixon").

57. See, for example, Regulations of State of Mississippi and Utah.

58. Dixon, Section 10.05[4].

59. Dixon, Section 10.05[6].

60. See, for example, Lindsay v. Ortho Pharmaceutical Corporation, 637 F.2d 87 (2d Cir 1980).

61. Dixon, Section 11.02[2].

62. Supra, note 35.

63. Dixon, Section 11.02[2].

64. Dixon, Section 11.02[4].

65. Schenebeck v. Serling Drug, Inc., 423 F. 2d 919 (8th Cir. 1970).

66. See generally, D. Louisell and H. Williams, 1 Medical Malpractice, Section 2.03 (Matthew Bender 1984).

67. Cf., Baker v. St. Agnes Hospital, 421 N.Y.S. 2d 81 (App. Div. 1979).

68. Texas Business and Commerce Code, Sections 2.313(a)(1) and 2.313(a)(2)("UCC")

69. UCC, Section 2.314.

70. UCC, Section 2.315.

71. UCC, Section 2.318. "These matters [of privity] are left for the courts to their determination."

72. See e.q., Texas Business and Commerce Code, Section 26.01(8) which requires a warranty or promise of cure to be in writing and signed by the person making the promise. Pharmacists are specifically excluded from this requirement.

73. Towsend v Catalina Ambulance Co., Inc. 857 S.W. 2d 791 (Corpus Christi 1993).

74. Texas Business and Commerce Code Section 17.41 et seq.

75. Id., Section 17.46(b)(5).

76. Id., Section 17.50(a)(1) and (2).

77. Supra, note 5.

78. See e.q., Texas Tort Claims Act, Texas Civil Practice and Remedies Code, Section 101.001 et seq.

79. Section 41-59-1, Mississippi Code of 1972, as amended.

80. Mississippi EMS: The Law, Rules and Regulations, Mississippi State Department of Health, Division of Emergency Medical Services, 1993 edition.

81. An Assessment of Mississippi Emergency Medical Services, National Highway Traffic Safety Administration Technical Assistance Team, June 4-6, 1991.

82. Tennessee Department of Health, Division of Emergency Medical Services, October, 1994.

83. Utah Administrative Rules, R426-3, Section 2.1.4.3.1., Utah Department of Health, Bureau of EMS, January 1994 Edition.

84. Personnel communication with Leslie Johnson, Utah Department of Health, Bureau of EMS, September, 1994.

85. Personnel communication with Captain Tim Hynes, Salt Lake City Fire Department, September, 1994.

86. Personnel communication with Jan Buttrey, Director, Bureau of EMS, Utah Department of Health, October 11, 1994.

87. Personnel communication with Joe Phillips, Tennessee Department of Health, Division of EMS, September, 1994.

88. L. Massingle, D. Manis, G. Messor, “Survey of Emergency Medical Services in Tennessee,” Journal of the Tennessee Medical Association 48.11 (1991); 535-541.

89. M. Smith, “The Drug Box Chill-Out,” Journal of Emergency Medical Services 17:10

(1992); 81-82.

APPENDIX A

The following is an excerpt from the Mississippi Rules and Regulations manual. This excerpt addresses drug associated standard pertinent to this report.

Note: ALS services are required to have ALS equipment commensurate with the ALS Staffing plan submitted as part of the application for service licensure.

(c) EMT-Intermediate

For the EMT-I, all the equipment for the EMT-B as previously listed plus the following equipment and supplies:

(1) Intravenous administration equipment (fluid should be in bags, not bottles), ringers lactate and/or normal saline (4000 ML minimum) dextrose (5%) in water 250 cc bags, (2 each minimum) intravenous administration set (3 each), intravenous catheter with needle (1"-3" in length; 22, 20, 28,16, 14 gauge 6 each minimum), venous tourniquet, antiseptic solution, IV pole or roof hook.

(d) EMT-Paramedic

All the equipment and supplies listed above plus the following additional equipment and supplies..

(3) *Drugs (pre-load when available)*

Drugs used on EMT-P units should be compatible with the minimum standards set by the Department of Transportation. The following drugs are required: Sodium Bicarbonate, Calcium Chloride, Epinephrine, Isoproterenol, Furosemide, 50% Dextrose, Activated Charcoal (USP), Bronchodilator, Dopamine, Atropine, Lidocaine, Nitroglycerine (spray or tablets), Naloxone, Diphenhydramine, Syrup of Ipec, Bretylium. The following drugs are optional: Diazepam, Morphine, Mannitol, Nifedipine capsules, Procainamide, Oxytocin, Thiamine, Verapamil, Doubtamine, Glucagon, Magnesium Sulfate, Aminophylline, Demerol, Levophed, Dexamethasone, Anitemetics and Nitrous oxide, Lorazepam, (Activan), Adenosine, (Adenocard), and Flumazenil (Mazicon).

**Any drug other than those specified here may be carried if previously approved and included in the medical control plan.*

Narcotics

Certified ALS personnel (paramedics and RNs) functioning under approved medical control jurisdiction may be issued approved controlled substances for prehospital use upon the discretion of the off-line medical director. For ALS services that are not hospital-based, the Drug Enforcement Administration (DEA) requires the off-line medical director to secure a separate CONTROLLED SUBSTANCES REGISTRATION CERTIFICATE to store, issue and prescribe controlled substances to ALS personnel. This CERTIFICATE should list the medical director as a "practitioner" at the physical address of the ambulance service where the drugs are stored. The off-line medical director will determine who may issue and administer the controlled substances and who will have access to storage of these narcotics.

Controlled substances must be secured in accordance with applicable state and federal regulations. The paramedic's narcotics should be secured in a designated location when he is not on duty and actively functioning under the service's medical control. When on duty, each paramedic should keep his controlled drugs in his immediate possession or securely locked in the vehicle at all times.

Whenever an order is received from medical control for administration of a narcotic, the paramedic must keep track of the vial/ampule being utilized. If the full amount of the narcotic was not administered, the remainder must be wasted in the presence of a witness and the witness must sign the patient report documenting same. The witness should preferably be a licensed health care provider who is authorized to administer narcotics themselves.

Narcotics should be replaced and logged within 24 hours of administration. Narcotics logs should be maintained by the ALS service. Paramedics should individually document the following minimum information in the narcotics log:

Date of administration
Time of administration
Amount administered
Amount wasted
Witness to wasted amount
Patient's name
Call number
Ordering physician

Any paramedic/RN who is separated from the ALS service's medical control authority shall surrender his narcotics upon demand or be subject to prosecution under applicable statutes.

Prescription Items

ALS ambulance services listed by DEMS are required to have approved medical directors. BLS ambulance services are required to have designated medical advisors. These physician directors and advisors are necessary to allow the services to store and administer certain prescription items as required in the Rules and Regulations

DEMS. Generally, only ALS licensed services are allowed to store and administer medications or other items that are labeled "Caution: Federal law restricts this device to sale by or an order of a physician." Some exceptions would be for BLS services to store and administer sterile water for irrigation or medical oxygen and oxygen administration devices, all of which are technically prescription items. Other exceptions may be approved by DEMS but these exceptions must be authorized and approved by the BLS service's physician medical director.

Storage of Prescription Items

Ambulance services and personnel should not store or carry prescription drugs or items which they are prohibited from using. Personnel who are allowed to administer prescription drugs or use prescription or use prescription items should carry these drugs and/or items only when they are on duty and actively functioning under their ambulance service's medical control authority.

Prescription items and drugs should always be stored and carried in secure locations accessible only to authorized personnel. ***These items and drugs should be stored within temperature ranges as recommended by the manufacturer.***

APPENDIX B

Robert C. Kellow is Chairman of the Board and Chief Executive Officer of EMERTECH Incorporated, Ft. Worth, Texas and Tucson, Arizona. He has held several senior EMS administrative positions, including Director of Emergency Medical Services with the American College of Emergency Physicians. Throughout his twenty-six year career in the EMS field, he has served on numerous national committees and board in the fields of health policy, education, EMS administration, medicine and government. In addition to his national and international consultancies, he is an inventor, author, researcher and lecturer. He is a recipient of the Rocco V. Morando Lifetime Achievement Award from the National Association of Emergency Medical Technicians and EMS Leadership Award from the American College of Emergency Physicians' Emergency Medical Services Committee.

Carter L. Ferguson, JD, is a shareholder in McLean & Sanders, a professional corporation, engaged in the practice of law in Fort Worth, Texas. His practice encompasses merger and acquisition services, counseling in business transactions and representing officers and directors of corporations. He received his law degree with honors form Texas Tech University School of Law in 1976. He currently serves on the Corporation Law Committee and the Limited Liability Company Committee of the Business Law Section of the State Bar of Texas. He is a Fellow in the Texas Bar Foundation. He is also a director of EMERTECH Incorporated.

Wade N. Spruill, Jr., is a 25 year veteran of the Mississippi State Department of Health. He has served as Director of the Division of Emergency Medical Services since 1974. He authored and steered the legislative adoption of the Mississippi EMS Act of 1974 and all subsequent amendments which include Advanced Life Support, EMS Fees, EMS Operating Fund, the Good Samaritan Law, The Mississippi Trauma Systems Law, and assisted in the passage of seat belt, road numbering system, and the telecommunications laws. He is the legislative liaison for Mississippi Public Health Association, President of Mississippians for EMS, Charter member of the Mississippi EMT Association and the Mississippi Society of Certified Public Managers. Nationally he is faculty for the National Highway Traffic Safety Administration's Development of Trauma Systems curriculum, consultant to NHTSA for the Emergency Vehicle Operators Training Program, member of the NHTSA Technical Assessment Program, member of the National Emergency Medical Services for Children Resource Alliance Board and the National Association of State EMS Director.